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EXAMINER

NAFF, DAVID M

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1657

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/626,459

Applicant(s)

MIZUNO ET AL.

Examiner

David M. Naff

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 1/30/07 & 5/16/07.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4-9, 13-17, 23, 24, 27, 30-33 and 35-37 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 4-9, 13-17, 23, 24, 27, 30-33 and 35-37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

An amendment of 1/30/07 in response of a office action of 10/4/06 amended claims 4, 6, 7, 19, 22 and 23, canceled claim 12, and added new claims 29-37.

5 A response of 5/16/07 to a restriction requirement of 4/20/07 elected with traverse Group I claims 4-9, 13-17, 21, 23-28 and 30-37.

The response also amended claims 4-9, 13, 14, 23, 24, 27, 30 and 33. Claims 1-3, 10-12, 18-22, 25, 26, 28, 29 and 34 have been canceled.

10 Since non-elected claims 19, 22 and 29 have been canceled, the traverse of the restriction requirement is moot.

The response to the restriction requirement requests that a species election requirement be withdrawn. However, the restriction did not contain a requirement for election of species.

15 Claims examined on the merits are 4-9, 13-17, 23, 24, 27, 30-33 and 35-37, which are all claims in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

20 Claim 30 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 24. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

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Claim Rejections - 35 USC § 112

Claims 4-9, 13-17, 23, 24, 27, 30-33 and 35-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which
5 was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Support is not found in the specification for methods as required
10 by claims 23 and 30. The specification fails to describe expanding and suspending as required by step b) of the claims. The specification fails to describe using a plurality of conditions promoting activation and propagation that can each be used alone or in any combination as required in step d) of claims 23 and 30.

15 Support is not found in the specification for a range of about 0.01 MPa to about 10 MPa for applying hydrostatic pressure, a range of "about 1 to about 8 hours" for applying hydrostatic pressure, and a range of "16 to about 23 hours per day for applying a static atmospheric pressure in claims 23 and 30. The page and lines of the
20 specification where the ranges are recited should be pointed out.

Support is not found in the specification for step b) of claims 23 and 30, i.e. both expanding and suspending in collagen, collagen gel, collagen sol, or a collagen-containing solution.

Support is not found in the specification for collagen containing
25 materials as recited in claim 4. The specification (paragraph

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bridging pages 11 and 12) discloses cell-contracted collagen containing proteoglycans, glycosaminoglycans or glycoproteins. Support is not found for collagen other than cell-contracted collagen containing containing proteoglycans, glycosaminoglycans or glycoproteins. Additionally, the specification fails to support that materials other than proteoglycans, glycosaminoglycans or glycoproteins recited in the paragraph are to be contained by cell-contracted collagen.

Support is not found in the specification for a range of "about one to about 28 days" at an atmospheric pressure as in claim 14. The page and line where this range is recited should be pointed out.

Support is not found in the specification for superficial cartilage layer integrated into a synovial membrane as required by claim 27.

Support is not found in the specification for further limiting a method as required by claim 30 as required by claims 31-33 and 35-37.

Response to Arguments

Page 12 of an amendment of 1/30/07 points to pages of the specification as providing support. However, these pages do not describe a method as recited by claims 23 and 30, and describe ranges and other conditions noted above that support is lacking.

Claim Rejections - 35 USC § 112

Claims 4-9, 13-17, 23, 24, 27, 30-33 and 35-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to

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particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 23 and 30 and other claims noted above not having support in the specification are confusing and unclear by claiming methods not described in the specification. Claiming several different procedures for activation for use each alone or in combination in step d) of the claims especially makes the claims unclear since the alternative procedures differ substantially such that selecting one procedure or a combinations of procedures will result in a substantially different method than when using another activation procedure or another combination of activation procedures. Furthermore, setting forth pressure and time period for hydrostatic pressure and static atmospheric pressure, flow rate and percent oxygen is confusing since hydrostatic pressure, static atmospheric pressure, flow rate and oxygen content are alternative to each other and to other activation procedures and do not have to be used for activation in step d). For example, activation can result from only temperature, length of time, cell density, carbon dioxide content, or any combination of these.

Step b) of claims 23 and 30 are confusing by requiring expanding and suspending in the same step. Expanding and suspending are separate steps, and cannot be performed at the same time. Furthermore, it is uncertain as to steps that constitute "expanding", and it is not seen how expanding and suspending can be in collagen or a collagen gel since these are solid materials.

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Claims 23 and 30 are further unclear by requiring cells that could be differentiated into chondrocytes in step a) since all of the subsequent steps relate only to chondrocytes.

Requiring constant hydrostatic pressure to have an Hz range is
5 confusing since it is not seen how constant pressure can change to have an Hz range.

Claim 24 in line 5 is confusing by reciting "may be" since such language does not require the sealant to be that recited. Additionally, --- bottom adhesive --- should be recited before
10 "sealant" in line 5 of the claim to be clear that the sealant is the bottom adhesive sealant.

Claim 30 in step f) is unclear by not having clear antecedent basis for "the neo-cartilage". Additionally, in step g) there is not clear antecedent basis for "the polyethylene glycol cross-linked with
15 methylated collagen".

Claims 31 and 32 are unclear by requiring the top or bottom sealant to be selected from a group of materials since claim 30 limits the top sealant to polyethylene glycol cross-linked with methylated collagen. In claim 30 the top sealant cannot be a material other than
20 polyethylene glycol cross-linked with methylated collagen, and a dependent claim that encompasses the top sealant being another material is improper.

Claim 35 is unclear by depending on canceled claim 34. There is not antecedent basis for "said perfusion flow rate" in line 2 of claim
25 35.

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Claim 37 is unclear by not having antecedent basis for "said perfusion and pressure" in line 2. Claim 36 does not require both perfusion and pressure.

Response to Arguments

5 An amendment of 1/3/07, urges that amendments to the claims have obviated indefiniteness. While some indefiniteness has been obviated by amendments of 1/3/07 and 5/16/07, indefiniteness still remains, and in certain instances amendments and/or addition of claims has resulted in additional indefiniteness.

10 ***Claim Rejections - 35 USC § 103***

Claims 4-6, 13-17, 23 and 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al (6,528,052 B1) in view of Wise et al (American Surgeon) and Rhee et al (5,475,052), and if necessary in further view of Rhee et al (5,565,519).

15 The claims are drawn to a method for treatment of a cartilage lesion and formation of a superficial cartilage layer by surgically implanting a cartilage construct into the lesion, and covering the construct with a layer of a top adhesive sealant that is polyethylene glycol (PEG) cross-linked with methylated collagen. In claim 23 the
20 method is carried out by isolating chondrocytes from cartilage, expanding and suspending the chondrocytes, seeding the chondrocytes suspension into a support matrix, preparing a construct for
25 implantation by subjecting the seeded support to conditions that promote activation and propagation of the chondrocytes, implanting the construct in a cartilage lesion, and depositing over the construct a

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top adhesive sealant that is PEG cross-linked with methylated collagen, which results in formation of a superficial cartilage layer over growing the implanted construct.

Smith et al disclose formation of cartilage tissue *in vitro* from
5 chondrocytes and implanting the cartilage (col 9, lines 22-33). The cartilage is formed by isolating cartilage cells, and culturing the cells while in a scaffold or support (col 9, line 30). The resultant cartilage tissue is transferred to a defect (col 9, lines 35-40).

Wise et al disclose using a collagen-polyethylene glycol sealant
10 to seal leaks after liver transplantation.

Rhee et al ('052) disclose using a collagen-polyethylene glycol matrix (cols 15-17 and col 20, line 60 to col 23, line 67) for implant applications.

Rhee et al ('519) disclose using a collagen-polyethylene glycol
15 conjugate for ophthalmic applications (cols 9-20)

It would have been obvious to seal a defect after implanting cartilage tissue in a defect as disclosed by Smith et al using a collagen-polyethylene glycol sealant as suggested by Wise et al using this sealant and Rhee et al using a collagen-polyethylene glycol
20 matrix for implant applications. It would have been obvious that sealing the defect after implanting will be advantageous to prevent contamination and infection at the site of the defect. The cartilage produced by Smith et al before implanting is inherently a construct. If needed Rhee et al ('519) would have further suggested using a
25 collagen-polyethylene glycol sealant from disclosing using a collagen-

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polyethylene glycol conjugate for ophthalmic applications. The activation procedures in claim 23 are alternative and do not have to be by using cyclic or constant hydrostatic pressure, static atmospheric pressure, flow rate or oxygen percent, and the specific conditions for these activation procedures are not required by claim 23. In any event, a hydrostatic pressure as in claim 23 is disclosed by Smith et al. Methylated collagen in claim 23 is taught by Rhee et al ('052) (col 16, line 29). The parent application does not antedate Wise et al since the presently claimed invention is not disclosed in the parent application.

Response to Arguments

The amendment of 1/30/07 urges that Smith et al do not suggest a sealant. However, after implanting, a sealant would have been obvious to close the wound resulting from surgical implantation against the outside environment for the same reason that a bandage is placed on a wound. Formation of a superficial cartilage layer will be inherent as the defect heals. Smith et al is not applied alone, but in combination with Wise et al and Rhee et al ('052), and if needed Rhee et al ('519), and these references would have suggested a collagen-polyethylene glycol sealant. As to the argument concerning the use of a bottom layer of sealant, this layer is not required by claim 23. Additionally, cyclic or constant hydrostatic pressure, static atmospheric pressure, flow rate and oxygen percent are not required by claim 23 since these activation conditions are alternative to other activation conditions.

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Double Patenting

Claims 4-9, 13-17, 23, 24, 27, 30-33 and 35-37 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 6,528,052 B1 in view of Wise et al and Rhee et al (5,475,052), and if necessary in further view of Rhee et al (5,565,519).

For the type of reasons set forth above, it would have been obvious to seal a defect after implanting the in vitro formed cartilage of claim 16 of the patent using a sealant suggested by Wise et al and Rhee et al ('052), and if needed Rhee et al ('519). Formation of a superficial cartilage layer will be inherent when the defect containing the sealed implanted construct heals.

Response to Arguments

The type of response set forth above to arguments traversing the 103 rejection also applies to this rejection. The amendment of 1/30/07 urges that patent 6,528,052 is not applicants' patent. However, an inventor of the patented invention is R. Lane Smith, which is the same inventor as Robert Smith of the present invention. Therefore, there is a common inventor, and use of the patent in a double patenting rejection is proper.

Conclusion

Claims 7-9, 24, 27 and 30-33 are free of the prior art.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE**

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FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



David M. Naff
Primary Examiner
Art Unit 1657

DMN

15 8/4/07